Adipose tissue hypoxia is related to increased mtDNA copies and decreased VEGF-A in fat dairy cows

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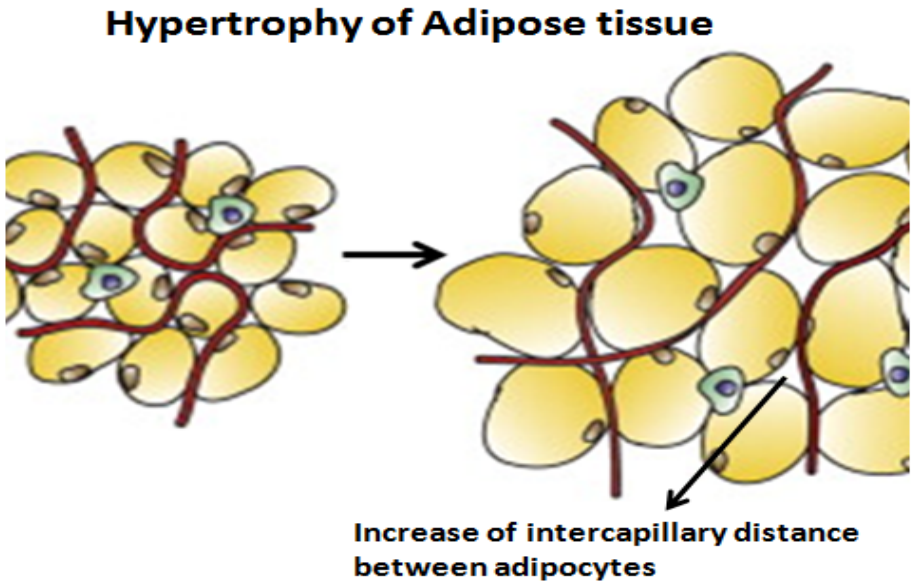
Adaption to Lactation in Dairy cows



Adapted from Yilmaz & Hotamisligil, 2013

Hypotrophy
Hypertrophy

abolic diseases:

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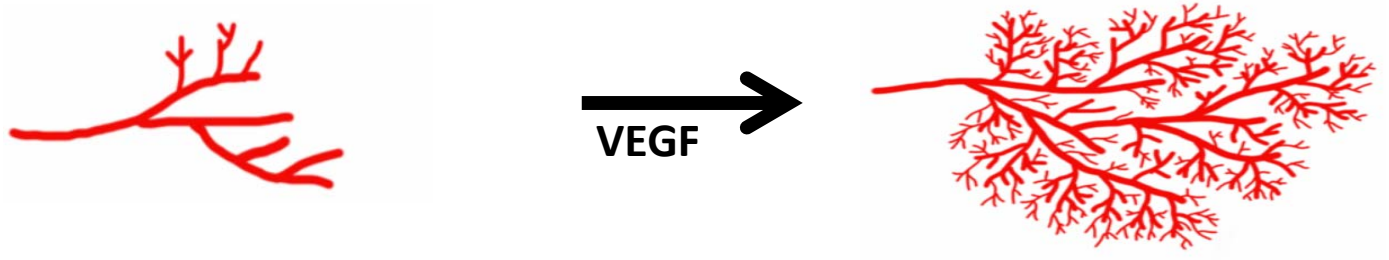
Angiogenesis

Formation of new capillaries and blood vessels from pre-existing ones



Vascular Endothelial Growth Factor A (VEGF-A):

- **key regulator of angiogenesis**
- **stimulates proliferation of endothelial cells**
- **upregulated through hypoxia in adipose tissue (AT)** (Zhang et al., 1997)
- **decreased VEGF-A protein amounts in fat dairy cows** (Laubenthal et al., 2014)

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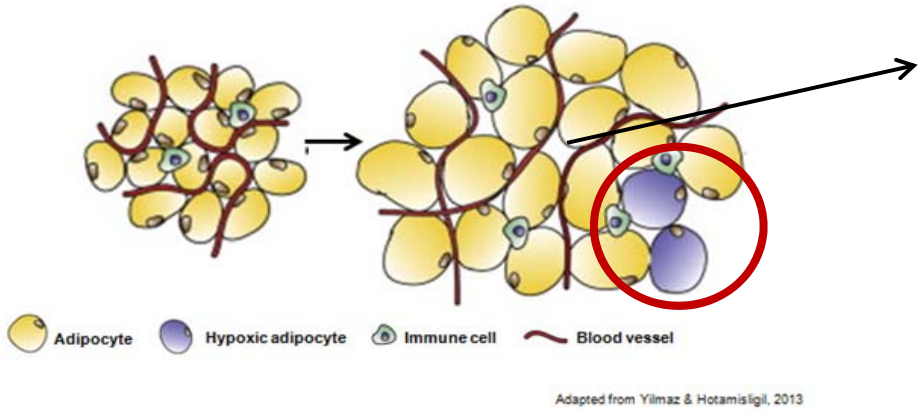
Hypoxia in AT

Insufficient oxygen supply of a body region



Adapted from Yilmaz & Hotamisligil, 2013

Increase of intercapillary distance between adipocytes

Hypoxia Inducible Factor-1α (HIF-1α)

- **major hypoxia marker** (Lemoine et al., 2013)
- **upregulated during hypoxia in obese humans and mice** (Mason et al., 2007)
- **induces VEGF-A in response to hypoxia** (Cao et al., 2007)

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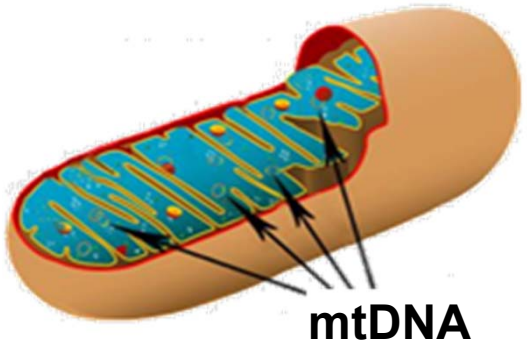
Mitochondrial DNA copy number

Mitochondria are the main site of energy production in AT



Mitochondrial DNA (mtDNA) copy number

= abundance of mitochondria per cell

- **modulated by physiological and environmental changes**
- **lipogenesis impairs mtDNA in human AT** (Kaaman et al., 2007)
- **increased mtDNA copy numbers in AT of overconditioned cows** (Laubenthal et al., 2014)

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Hypotheses

Decreasing angiogenesis in AT of overconditioned cows might lead to

<u>local hypoxia</u>

Compensation of hypoxic condition by increasing numbers of mitochondria

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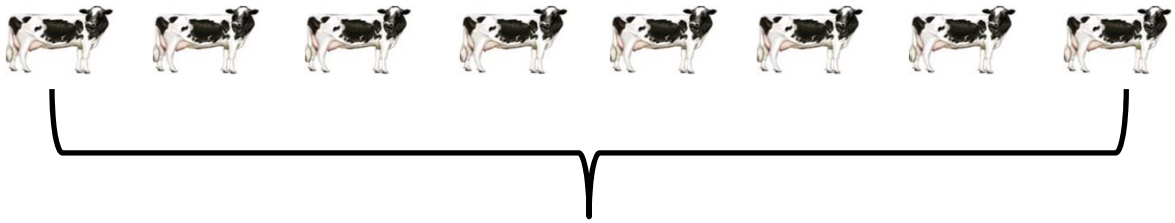
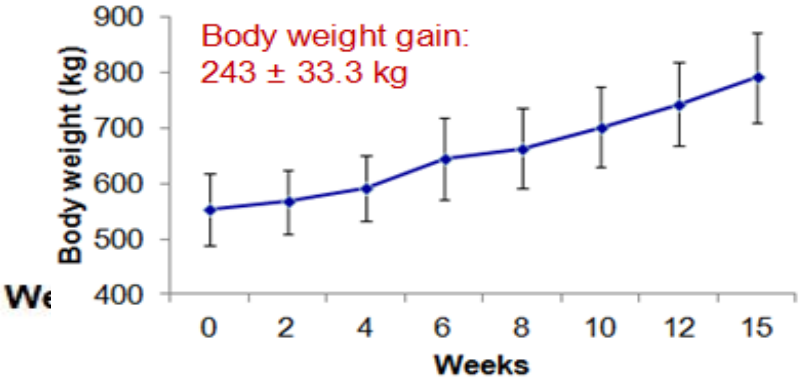
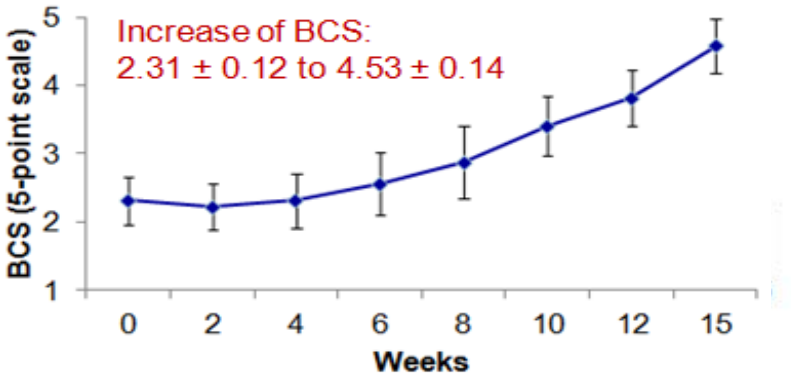
Experimental design



non-lactating; non-pregnant; 4 - 6 years; n = 8





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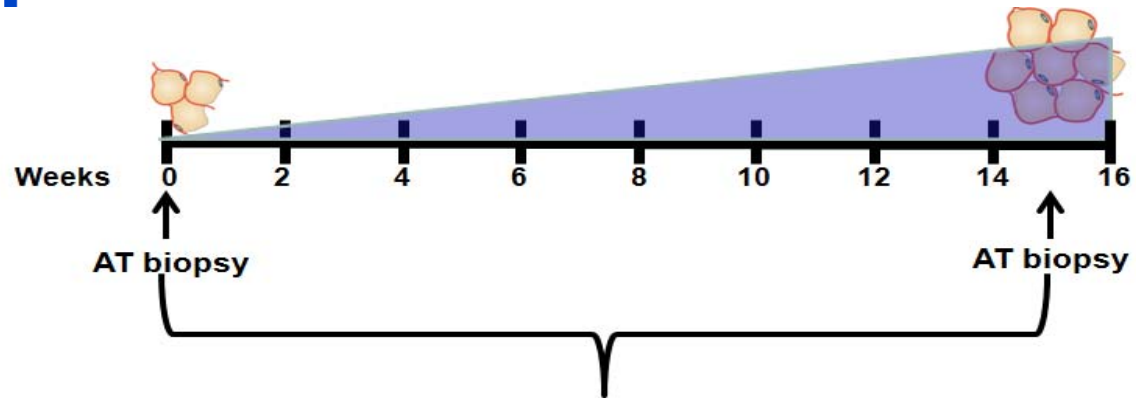
Material and Methods



HIF-1α	mtDNA copy number/cell	VEGF-A	Adipocyte area
Immunhistochemistry	**Multiplex qPCR**	**Western blot**	**Histology**
polyclonal rabbit anti HIF-1α	12S rRNA gene/β-globin gene	monoclonal mouse anti VEGF-A /mouse anti ß-actin	Area (µm²) of 100 randomly selected adipocytes

Statistics: non-parametric Wilcoxon-test, Spearman correlation coefficient (SPSS; mean ± SEM)

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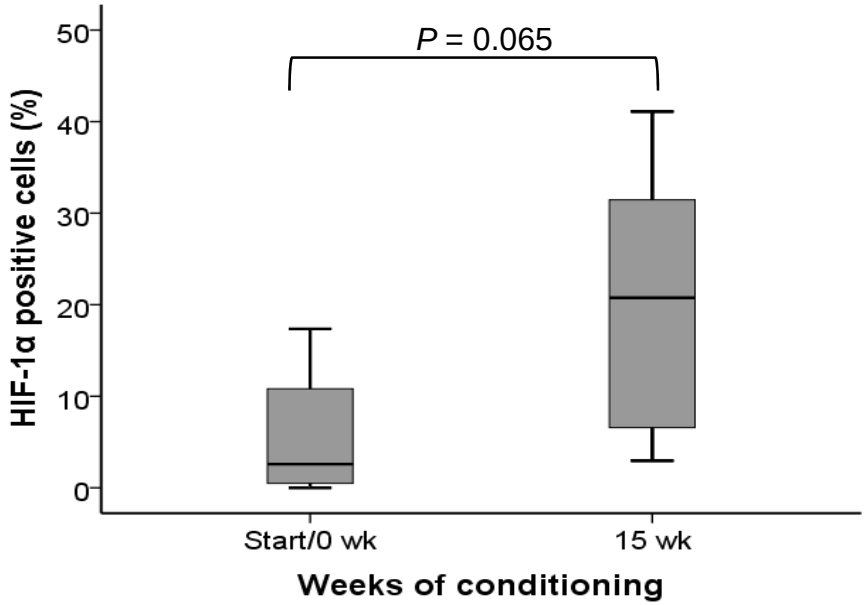
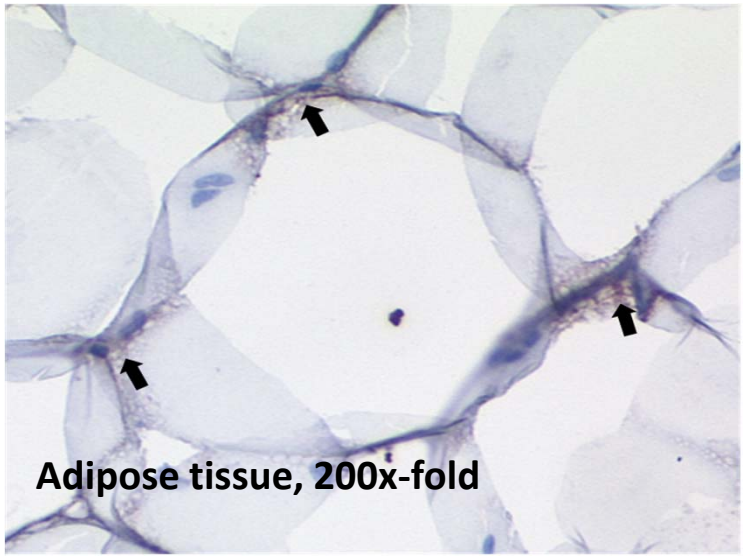
HIF-1α in AT of overconditioned cows





Local hypoxia in AT

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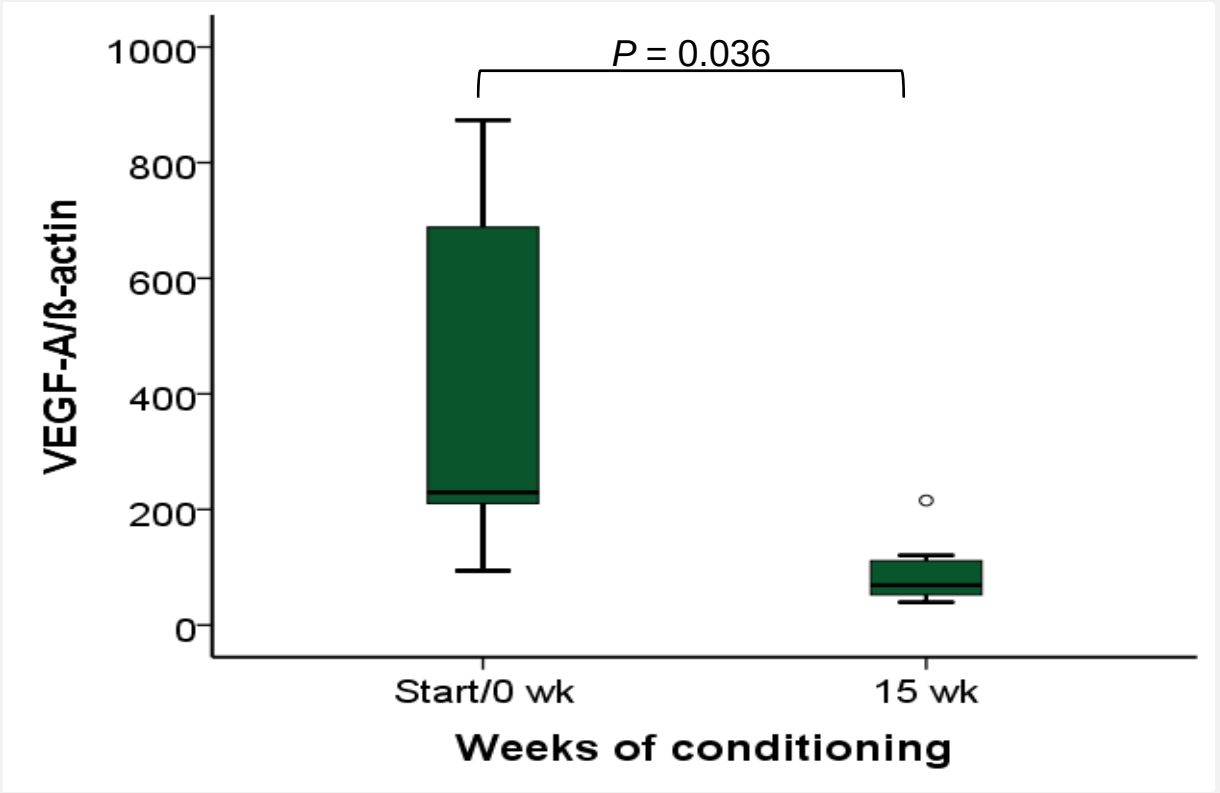
Relationships between HIF-1α and VEGFA, mtDNA and adipocyte area



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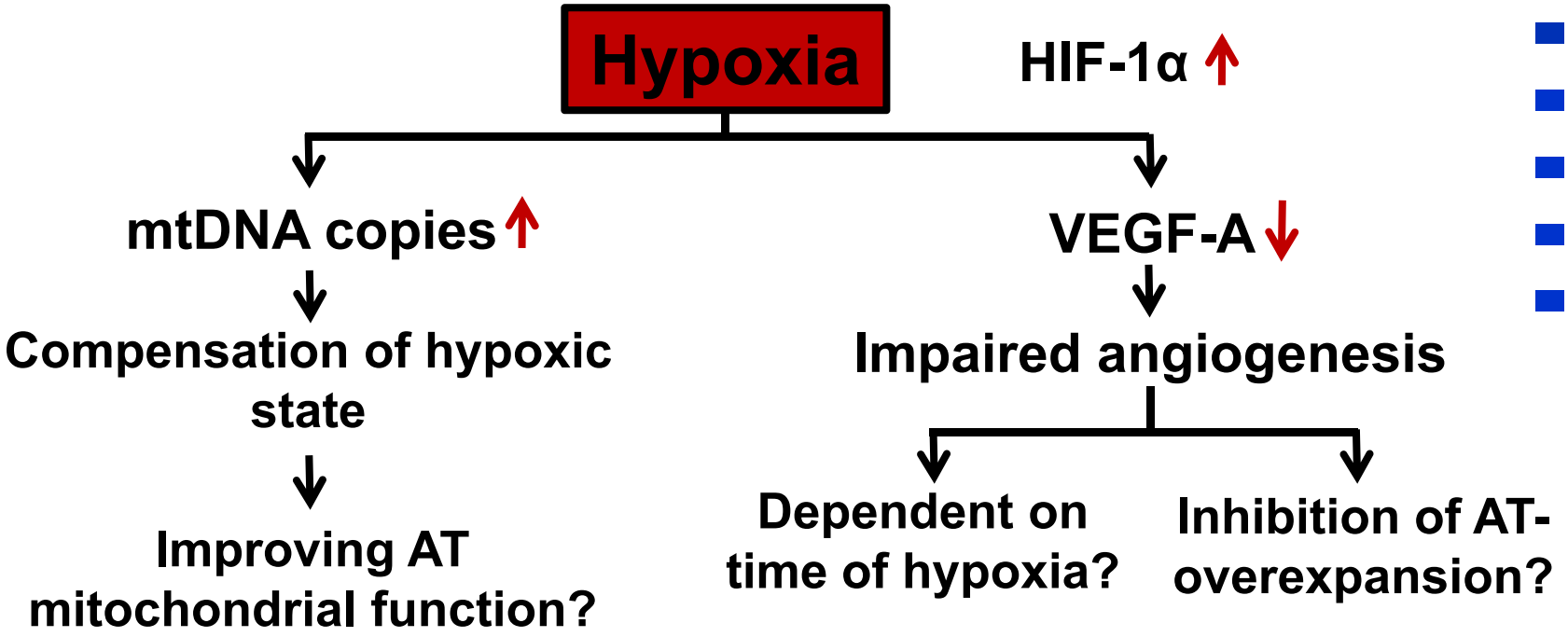
Summary & Conclusions



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Thanks for your attention

Thanks to EAAP for travel funding

Contact: lilian.laubenthal@uni-bonn.de

Week	Proportion of the daily ration (g/kg DM)			
	Straw	Corn silage	Grass silage	Concentrate
0	1000	0	0	0
1	731	110	73	86
2	497	199	132	172
3	297	267	178	258
4	131	315	210	344
5	0	342	228	430
6	0	290	194	516
7 - 16	0	240	160	600